SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Antibody to Hepatitis C Virus (Anti-HCV) Rapid Assay

Device Trade Name: OraQuick® HCV Rapid Antibody Test

Applicant's Name and Address: OraSure Technologies, Inc.
220 East First Street
Bethlehem, PA 18015

Date of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P080027/S001

Date of FDA Notice of Approval: February 18, 2011

Expedited: Not Applicable

The original PMA (P080027) was approved on 06/25/2010 and is indicated for "The OraQuick® HCV Rapid Antibody Test is a single-use immunoassay for the qualitative detection of antibodies to hepatitis C virus (anti-HCV) in venipuncture whole blood specimens (EDTA, sodium heparin, lithium heparin, and sodium citrate) from individuals 15 years or older. The OraQuick® HCV Rapid Antibody Test results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive evidence of infection with HCV (state of infection or associated disease not determined) in persons with signs or symptoms of hepatitis and in persons at risk for hepatitis C infection." The current supplement was submitted to expand the indication for the OraQuick® HCV Rapid Antibody Test to the use of fingerstick whole blood in the assay.

II. INDICATIONS FOR USE

The OraQuick® HCV Rapid Antibody Test is a single-use immunoassay for the qualitative detection of antibodies to hepatitis C virus (anti-HCV) in fingerstick whole blood specimens and venipuncture whole blood specimens (EDTA, sodium heparin, lithium heparin, and sodium citrate) from individuals 15 years or older. The OraQuick® HCV Rapid Antibody Test results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive evidence of infection with HCV (state of infection or associated disease not determined) in persons with signs or symptoms of hepatitis and in persons at risk for hepatitis C infection.

CONTRAINDICATIONS

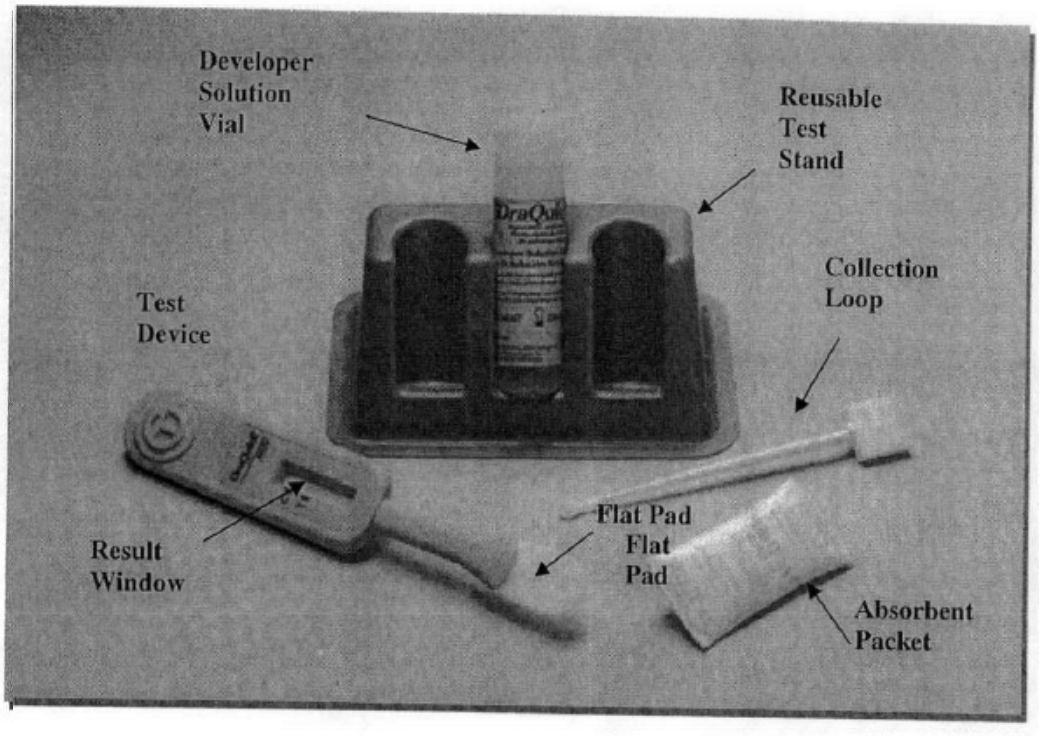
None

III. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the OraQuick® HCV Rapid Antibody Test labeling.

IV. DEVICE DESCRIPTION

The OraQuick® HCV Rapid Antibody Test kit is comprised of a divided pouch containing a test device with an absorbent packet and a labeled developer solution vial. Also included in the kits are reusable test stands, single use specimen collection loops, and a package insert.



The OraQuick® HCV Rapid Antibody Test utilizes an indirect lateral flow immunoassay method to detect antibodies to both structural and non-structural HCV proteins. The device utilizes synthetic peptides and recombinant antigens from the core, NS3, and NS4 regions of the HCV genome, that are immobilized as a single test line on the assay strip. Antibodies reacting with these peptides and antigens are visualized by colloidal gold labeled with protein A generating a visible line in the test zone for a reactive sample. The device also includes a built-in procedural control that demonstrates assay validity. A reddish-purple line in this Control Zone (C Zone) must appear for a test result to be valid, whether or not the sample is reactive or non-reactive for anti-HCV.

The OraQuick® HCV Rapid Antibody Test Kit Controls are available separately for use only with the OraQuick® HCV Rapid Antibody Test. The Kit Controls are human plasma-based reagents and are specifically formulated and manufactured to ensure proper performance of the test. The HCV Positive Control will produce a reactive reddish-purple line at the Test Zone (T Zone). The HCV Negative Control will generate a non-reactive

test result (no reddish-purple line at the T Zone). Use of kit control reagents manufactured by any other source may not meet the requirements for an adequate quality assurance program for the OraQuick® HCV Rapid Antibody Test.

V. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the detection of antibodies to HCV. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

Determination of the presence of anti-HCV in patients may be achieved by using a variety of commercially available FDA approved serological tests. Anti-HCV test results are used in combination with a physician's assessment and other laboratory test results, in order to establish a diagnosis of infection with HCV.

VI. MARKETING HISTORY

The product has been commercialized in the countries comprising the European Union. This product has not been withdrawn from any market for any reason. The (device) has not been marketed in the United States with the whole blood fingerstick specimen claim.

VII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

A false positive result using an anti-HCV test would not be considered a patient or public health concern since a reactive result would be followed-up with supplemental tests, e.g., polymerase chain reaction (PCR) for detection of HCV RNA and/or strip immunoblot assay (SIA) to confirm infection and/or determine disease state. Treatment of the patient with chronic HCV infection is initiated only after extensive clinical, laboratory and behavioral assessment in order to assess eligibility and ability to comply with therapy.

A false negative anti-HCV result in a diagnostic setting may cause an HCV infected patient to remain undetected. This could be a safety concern for both the patient and the public, since such individuals may be capable of transmitting HCV infection. However, in patients where the suspicion of HCV infection is high, HCV RNA testing is often used to identify viremic individuals.

There were no adverse events that occurred in the clinical studies.

VIII. SUMMARY OF PRECLINICAL STUDIES

The performance characteristics of the OraQuick® HCV Rapid Antibody Test were evaluated in the non-clinical studies performed at OraSure Technologies, Inc.

A. Laboratory Studies

Biocompatibility

The OraQuick® HCV device housing biocompatibility testing was completed by NAMSA (North American Science Associates) located at 6750 Wales Road, Northwood, Ohio. All testing was compliant with FDA Good Laboratory Practice (GLP) Requirements 21 CFR part 58. All testing used the OraQuick® HCV device housings (Top PN 3001-1745 and Base PN 3001-1746).

Reactivity with HCV Seroconversion Panels

Eighteen panels containing sequential plasma specimens from individuals undergoing seroconversion as a result of HCV infection were evaluated with the OraQuick® HCV Rapid Antibody Test and compared with an FDA approved anti-HCV EIA test. The OraQuick® HCV Rapid Antibody Test and the reference anti-HCV assay results are summarized in the following table. The sensitivity of the OraQuick® HCV Rapid Antibody Test to detect seroconversion was similar to that of the comparator EIA. The OraQuick® HCV Rapid Antibody Test detected anti-HCV antibodies earlier than the EIA in 9 of the 18 seroconversion panels (50%) and by an overall average of 3.6 days (95% CI = 1.2 to 5.9).

Seroconversion Panel	Days to Evidence of HCV Infection				
	OraQuick® HCV Rapid Antibody Test		FDA approved anti-HCV EIA		Difference (OraQuick® - EIA) First Reactive
	Last Non-Reactive	First Reactive	Last Non-Reactive	First Reactive	
HCV 6213	35	37	30	37	0
HCV 6214	18	23	23	25	-2
HCV 6227	46	74	46	74	0
HCV 9041	31	62	31	62	0
HCV 9046	0	69	0	69	0
HCV 9047	21	28	21	28	0
PHV 901	65	97	65	97	0
PHV 905	7	11	11	18	-7
PHV 907	7	13	13	18	-5
PHV 910 (M)	0	4	0	4	0
PHV 911 (M)	0	11	0	11	0
PHV 914	9	12	19	24	-12
PHV 916 (M)	7	9	9	23	-14
PHV 917 (M)	22	85	22	85	0
PHV 920	7	13	7	16	-3
PHV 921	0	4	4	14	-10
RP 006	388	461	461	469	-8
RP 038	47	52	52	55	-3
Average		**59.2**		**62.7**	**-3.6 (-5.9 to -1.2)**

Reactivity with HCV Specimens from Various Genotypes and Subtypes

The ability of the OraQuick® HCV Rapid Antibody Test to detect infection derived from various genotypes and subtypes was assessed using two commercially available Worldwide HCV Performance panels. Thirty-two HCV-positive plasma specimens derived from multiple geographic regions, representing four genotypes (1, 2, 3 and 4) were tested. All specimens were reactive with the OraQuick® HCV Rapid Antibody Test. Three HCV-negative samples were included in the panel and all were non-reactive with the OraQuick® HCV Rapid Antibody Test.

Interfering Substances

The OraQuick® HCV Rapid Antibody Test was evaluated with the following interfering substances present in whole blood samples in order to assess their potential effect on the assay performance as per CLSI guidelines EP7-A2. Testing was completed on ten HCV-negative whole blood samples and ten HCV-positive spiked matched whole blood samples. All matched samples were spiked according to one of the following conditions as per the table below:

Interfering Substances	Concentration
Bilirubin	10 mg/dL
Hemoglobin	500 mg/dL
Lipid (Triolein)	3500 mg/dL
Protein	12 g/dL

None of these interfering substances had any impact on the OraQuick® HCV Rapid Antibody Test assay performance at the concentrations evaluated.

Medical Conditions Unrelated to HCV Infection

The performance of the OraQuick® HCV Rapid Antibody Test was evaluated with commercially available HCV negative plasma and serum specimens derived from patients with medical conditions unrelated to HCV infection. Results are summarized in the table below.

Medical Condition		Non-Reactive (%)	Reactive (%)
Autoimmune Diseases	**N**		
Myasthenia Gravis	4	4 (100)	0 (0)
Rheumatoid Arthritis	10	10 (100)	0 (0)
Systemic Lupus Erythematosus (SLE)	*10*	*10 (100)*	0 (0)
Other Medical Conditions			
Influenza Vaccination	10	10 (100)	0 (0)
Hepatitis A Virus (HAV)	59	59 (100)	0 (0)
Hepatitis B Virus (HBV)	58	58 (100)	0 (0)
Hepatitis D Virus (HDV)	*2*	*2 (100)*	0 (0)
Hepatitis E Virus (HEV)	8	8 (100)	0 (0)
Epstein-Barr Virus (EBV)	10	10 (100)	0 (0)
Cytomegalovirus (CMV)	10	10 (100)	0 (0)
Herpes Simplex Virus (HSV)	10	10 (100)	0 (0)
Parvovirus B19	*10*	*10 (100)*	0 (0)
Rubella	10	10 (100)	0 (0)
Syphilis	10	10 (100)	0 (0)
Toxoplasmosis	10	10 (100)	0 (0)
Human Immunodeficiency Virus (HIV-1/2)	154	154 (100)	0 (0)
Heterophilic antibodies	*10*	*10 (100)*	0 (0)
Multiparous Female	10	10 (100)	0 (0)
Total Samples Tested	**405**	**405**	**0**

None of the medical conditions tested produced false positive results in the OraQuick® HCV Rapid Antibody Test device. Performance characteristics in scleroderma, Sjögren's Syndrome and Human T-Cell Lymphotropic Virus (HTLV I/II) have not been established.

Sample Stability

The OraQuick® HCV Rapid Antibody Test was evaluated with whole blood stored at various storage conditions over numerous days. Results are summarized in the table below.

Specimen Type	Days at Storage Condition	
	2°-8°C (36°-46°F)	15°-30°C (59°-86°F)
Whole Blood	7	3

Storing whole blood for up to 7 days refrigerated or 3 days at 15°-30°C (59°-86°F) did not impact the performance of the OraQuick® HCV Rapid Antibody Test.

Specimen Types

The OraQuick® HCV Rapid Antibody Test was evaluated with venipuncture whole blood samples collected in various types of anticoagulants including ethylenediaminetetracetic acid (EDTA), sodium heparin, lithium heparin, and sodium citrate. Testing was performed with twenty anti-HCV negative whole blood samples and twenty anti-HCV-spiked positive whole blood samples. Venipuncture whole blood in all anticoagulants produced acceptable assay performance. The recommended sample collection devices for use with the OraQuick® HCV Rapid Antibody Test in whole blood are vacuum tubes containing EDTA, sodium heparin, lithium heparin, sodium citrate.

Fingerstick whole blood is also an acceptable specimen type.

Limit of Detection Study

The limit of detection (LoD), defined as the EIA signal to cutoff ratio which yielded reactive results 95% of the time in the OraQuick® Rapid HCV Antibody Test device, was calculated for each of three (3) lots separately and for three (3) lots combined. Using values obtained with an FDA approved anti-HCV EIA, the LoD of the OraQuick® Rapid HCV Antibody Test for venous whole blood and fingerstick whole blood was calculated to be 0.75 and 0.89 s/co, respectively. This means that the OraQuick® HCV Rapid Antibody Test may provide a positive result where the comparator EIA is equivocal. Since the assay is visually read, the LoD may vary depending on the user (see tables below).

Venous Whole Blood

Anti-HCV positive whole blood dilutions were tested by three (3) operators over a period of five (5) day with three (3) lots of devices. For each dilution, a total of forty-five (45) data points were generated overall, or fifteen (15) data points per each of the three (3) device lots. The tables below summarize the number of reactive or non-reactive results obtained for the anti-HCV positive whole blood dilutions per device lot, per operator and overall.

OraQuick® HCV Device Test Results per Venous Whole Blood Dilution by Operator					
Plasma Dilution	Signal to Cutoff	Developer Dilution Assignment	Percent of Reactive Results per Operator		
			Operator 1	Operator 2	Operator 3
1:160	1.85	A	100% (15/15)	100% (15/15)	100% (15/15)
1:200	1.18	B	100% (15/15)	100% (15/15)	100% (15/15)
1:400	0.80	C	100% (15/15)	100% (15/15)	100% (15/15)
1:500	0.64	D	100% (15/15)	53.3% (8/15)	80.0% (12/15)
1:600	0.50	E	100% (15/15)	33.3% (5/15)	66.7% (10/15)

OraQuick® HCV Device Test Results per Venous Whole Blood Dilution by Lot					
Plasma Dilution	Signal to Cutoff	Developer Dilution Assignment	Percent of Reactive Results per Lot		
			Lot 1	Lot 2	Lot 3
1:160	1.85	A	100% (15/15)	100% (15/15)	100% (15/15)
1:200	1.18	B	100% (15/15)	100% (15/15)	100% (15/15)
1:400	0.80	C	100% (15/15)	100% (15/15)	100% (15/15)
1:500	0.64	D	73.3% (11/15)	73.3% (11/15)	66.7% (10/15)
1:600	0.50	E	66.7% (10/15)	73.3% (11/15)	60.0% (9/15)

Summary of OraQuick® HCV Device Test Results per Venous Whole Blood Dilution for all OraQuick® HCV Tests						
Plasma Dilution	Signal to Cutoff	Developer Dilution Assignment	Total Number of Tests	Number of Reactive Results	Number of Non-Reactive Results	Percent of Reactive Results
1:160	1.85	A	45	45	0	100%
1:200	1.18	B	45	45	0	100%
1:400	0.80	C	45	45	0	100%
1:500	0.64	D	45	32	13	71.1%
1:600	0.50	E	45	30	15	66.7%

Using an FDA approved anti-HCV EIA, the LoD for venous whole blood was calculated to be 0.75 s/co (by probit analysis).

Fingerstick Whole Blood

Three operators took fingerstick whole blood from at least 30 individuals over a period of five days. The study verified the enrolled individuals to be HCV negative. Following

each fingerstick, the study directed each operator to place the whole blood into one of the dilutions, stir the solution, insert the investigational device into the solution, and finally read off the result. The operators had no knowledge of the dilution level. After a period of five days, the study resulted in 21 measurements taken at each dilution level, 7 measurements for each operator.

OraQuick® HCV Device Test Results per Venous Whole Blood Dilution by Operator					
Plasma Dilution	Signal to Cutoff	Developer Dilution Assignment	Percent of Reactive Results per Operator		
			Operator 1	Operator 2	Operator 3
1:160	1.85	A	100% (7/7)	100% (7/7)	100% (7/7)
1:200	1.18	B	100% (7/7)	100% (7/7)	100% (7/7)
1:400	0.80	C	71.4% (5/7)	100% (7/7)	100% (7/7)
1:500	0.64	D	42.9% (3/7)	42.9% (3/7)	100% (7/7)
1:600	0.50	E	0% (0/7)	71.4% (5/7)	71.4% (5/7)

Summary of OraQuick® HCV Device Test Results per Fingerstick Whole Blood Dilution for all OraQuick® HCV Tests						
Plasma Dilution	Signal to Cutoff	Developer Dilution Assignment	Total Number of Tests	Number of Reactive Results	Number of Non-Reactive Results	Percent of Reactive Results
1:160	1.85	A	21	21	0	100%
1:200	1.18	B	21	21	0	100%
1:400	0.80	C	21	19	2	90.5%
1:500	0.64	D	21	13	8	61.9%
1:600	0.50	E	21	10	11	47.6%

Using an FDA approved anti-HCV EIA, the LoD for fingerstick whole blood was calculated to be 0.89 s/co (by probit analysis).

Reproducibility

The reproducibility of the OraQuick® HCV Rapid Antibody Test was tested at 3 sites using 3 lots of test devices twice a day for 5 days with 9 operators (3 per site). Three whole blood panel member types (negative, limit of detection (LoD), and low positive) were tested in 5 unique test kit types. Each test kit consisted of eight (8) blinded panel members that had various combinations of the 3 panel members in a randomized sequence. Panel members were blinded per operator, run, and device lot to ensure that the results of the panel member types were unpredictable to the operator. The LoD specimen was determined to be a 0.75 s/co by an FDA approved EIA. Overall concordance across operators, sites, and device lots was 98.9% for the negative specimen, 98.7% for the LoD specimen and 99.7% for the low positive specimen.

Stability Studies

Two stability studies, comprised of three (3) validation lots each, are ongoing to evaluate the OraQuick® HCV Rapid Antibody Test shelf life and the OraQuick® HCV Rapid Antibody Test Kit Control shelf life. The OraQuick® HCV Rapid Antibody Test Kit Control study also includes an open vial stability evaluation.

The data from the stability study for the OraQuick® HCV Rapid Antibody Test substantiates a shelf life of eighteen (18) months at storage conditions of 2° - 30°C (36° - 86°F).

The data from the stability study for the OraQuick® HCV Rapid Antibody Test Kit Controls substantiates a twelve (12) month shelf life at storage conditions of 2° - 8°C (36° - 46°F). Once opened, the OraQuick® HCV Rapid Antibody Test Kit Controls have an eight (8) week shelf life at storage conditions of 2° - 8°C (36° - 46°F).

Shipping Studies

The OraQuick® HCV Rapid Antibody Test (Pouched Assay – Device and Developer Solution) is packaged in 25-count or 100-count preprinted boxes including an equivalent number of loops for blood testing, reusable OraQuick® Test stands, and package insert.

A shipping study was performed to confirm that the external packaging configuration for the OraQuick® HCV Rapid Antibody Test provided a high probability of safe and intact arrival at its destination. The study was designed to confirm that the integrity of the packaging and its components could withstand the simulated shipping and handling stresses and to demonstrate that the shipping and handling stresses had no adverse effect on the OraQuick® HCV Rapid Antibody Test performance.

The OraQuick® HCV Rapid Antibody Test Kit Controls are comprised of an HCV Positive Control and an HCV Negative Control packaged in a Control Box with its Package Insert. The Control Box is then placed in an insulated outer shipping carton. A shipping study was performed to confirm that the external packaging configuration for the OraQuick® HCV Rapid Antibody Test Kit Controls provided a high probability of

safe and intact arrival at its destination. The study was designed to confirm that the integrity of the packaging and its components could withstand simulated shipping and handling stresses and to demonstrate that the shipping and handling stresses had no adverse effect on the OraQuick® HCV Rapid Antibody Test Kit Control performance.

B. Animal Studies

Not Applicable

C. Additional Studies

Not Applicable

IX. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

VENOUS WHOLE BLOOD

Expected Results for the Intended Use Population

Of the 1207 specimens tested in two OraQuick® HCV Rapid Antibody Test clinical studies of venipuncture whole blood, 88.2% (1064/1207) were from subjects at risk for hepatitis C infection but were asymptomatic and reported no current signs or symptoms of hepatitis, and 11.8% (142/1207) were from subjects with current signs or symptoms of hepatitis. One (1/1207) pregnant subject was enrolled without signs or symptoms of hepatitis or risk factors for hepatitis C infection. The 1207 individuals were enrolled from the following collection locations:

- 50.3% from Miami, FL
- 24.7% from Ft. Lauderdale, FL
- 13.6% from Fall River, MA
- 10.7% from Allentown, PA
- 0.7% from College Park, MD, San Francisco, CA, Dallas, TX, and Philadelphia, PA.

The OraQuick® HCV Rapid Antibody Test was reactive in 36.7% (443/1207) of subjects tested. There were no invalid OraQuick® HCV Rapid HCV Antibody Test results reported for the 1207 specimens tested (0/1207, 95% CI: 0.0%, 0.3%). Of the 1207 individuals tested, 33.1% (400/1207) were also self-reported HIV positive. The table below summarizes the distribution of OraQuick® HCV Rapid Antibody Test reactive, non-reactive, and invalid results for the 1207 specimens tested.

Age Range	Gender	OraQuick® HCV Rapid Antibody Test Results in High Risk Individuals							
		No signs or symptoms				Signs or symptoms			
		Reactive	Non-Reactive	Invalid	Total (n)	Reactive	Non-Reactive	Invalid	Total (n)
		n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	
0-9	F	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
	M	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
10-19	F	0 (0.0)	11 (1.0)	0 (0.0)	11	1 (0.7)	1 (0.7)	0 (0.0)	2
	M	0 (0.0)	14 (1.3)	0 (0.0)	14	0 (0.0)	1 (0.7)	0 (0.0)	1
20-29	F	11 (1.0)	29 (2.7)	0 (0.0)	40	1 (0.7)	9 (6.3)	0 (0.0)	10
	M	7 (0.7)	50 (4.7)	0 (0.0)	57	1 (0.7)	3 (2.1)	0 (0.0)	4
30-39	F	15 (1.4)	44 (4.1)	0 (0.0)	59	4 (2.8)	18 (12.7)	0 (0.0)	22
	M	23 (2.2)	56 (5.3)	0 (0.0)	79	4 (2.8)	4 (2.8)	0 (0.0)	8
40-49	F	53 (5.0)	97 (9.1)	0 (0.0)	150	7 (4.9)	8 (5.6)	0 (0.0)	15
	M	82 (7.7)	191 (18.0)	0 (0.0)	273	6 (4.2)	8 (5.6)	0 (0.0)	14
50-59	F	41 (3.9)	38 (3.6)	0 (0.0)	79	3 (2.1)	5 (3.5)	0 (0.0)	8
	M	137 (12.9)	117 (11.0)	0 (0.0)	254	23 (16.2)	9 (6.3)	0 (0.0)	32
60-69	F	6 (0.6)	5 (0.5)	0 (0.0)	11	1 (0.7)	9 (6.3)	0 (0.0)	10
	M	13 (1.2)	19 (1.8)	0 (0.0)	32	2 (1.4)	5 (3.5)	0 (0.0)	7
70-79	F	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	4 (2.8)	0 (0.0)	4
	M	1 (0.1)	4 (0.4)	0 (0.0)	5	1 (0.7)	2 (1.4)	0 (0.0)	3
80-89	F	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	1 (0.7)	0 (0.0)	1
	M	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	1 (0.7)	0 (0.0)	1
90-100	F	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
	M	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
Total (N)*		389 (36.6)	675 (63.4)	0 (0.0)	1064	54 (38.0)	88 (62.0)	0 (0.0)	142

- Does not include one pregnant woman enrolled without signs or symptoms of hepatitis or at risk for hepatitis C infection.

Venous Whole Blood Clinical Performance

Two multi-center prospective studies were conducted to evaluate the clinical performance of the OraQuick® HCV Rapid Antibody Test in subjects with signs or symptoms of hepatitis and subjects at risk for hepatitis C infection. These risk factors included past or present intravenous drug use, having received a blood transfusion or organ transplant prior to 1992, evidence of high-risk sexual behavior, being born to an HCV positive mother, having been on long-term hemodialysis, history of incarceration, and positive for HIV. Clinical performance was evaluated in venipuncture whole blood specimens from subjects prospectively enrolled at 8 geographically dispersed centers within the United States.

The population tested was African American (43.0%), Caucasian (37.7%), Hispanic/Latino (17.1%), as well as a small proportion of other ethnic groups (2.2%). The mean age was 45 years (age range: 15 to 84 years). Of the 1207 subject specimens tested, 436 were HCV infected, 762 were negative, and 9 specimens had the status of "Unable to Determine". HCV status was determined for each subject by EIA, with supplemental RIBA® and PCR assays as required. The table below summarizes the distribution of OraQuick® HCV Rapid Antibody Test reactive, non-

reactive, and invalid results in subject with HCV infected status per the reference laboratory testing algorithm.

OraQuick® HCV Rapid Antibody Test Results	Subject HCV Infected Status		
	Positive	Negative	Unable to Determine Infected Status
Positive	435	0	8
Negative	1	762	1
Invalid	0	0	0

Percent Positive and Negative Agreement Calculations

Percent positive and percent negative agreement between the OraQuick® HCV Rapid Antibody Test and HCV status were calculated overall for the analysis population (n=1207), as well as for subjects with signs or symptoms of hepatitis and subjects at risk for hepatitis C infection.

$$\text{Percent Positive Agreement} = \frac{\text{Number of OraQuick® HCV Rapid Antibody Test Reactive Results}}{\text{Total number of HCV Infected status}} \times 100$$

$$\text{Percent Negative Agreement} = \frac{\text{Number of OraQuick® HCV Rapid Antibody Test Non-Reactive Results}}{\text{Total number of HCV Not Infected status}} \times 100$$

For the purposes of calculating percent agreement, OraQuick® HCV Rapid Antibody Test reactive results for samples whose HCV status was "Unable to Determine" following EIA with supplemental RIBA® and PCR testing were considered "HCV Not Infected", and OraQuick® HCV Rapid Antibody Test non-reactive results for samples whose HCV status was "Unable to Determine" following EIA with supplemental RIBA® and PCR testing were considered "HCV Infected".

Percent Positive and Negative Agreement

The percent positive and negative agreement between the OraQuick® HCV Rapid Antibody Test and the subject HCV Infected Status were calculated for the per protocol population (n=1207). Percent positive and negative agreements were also calculated for individuals with signs or symptoms of hepatitis (n=142), and for individuals at risk for hepatitis C infection (n=1064). Percent positive and negative agreements according to risk factors for HCV infection were also calculated. The risks for HCV were ranked on a clinical evaluation of the likelihood of acquiring hepatitis C, with the most common given higher rankings.[3] Each subject was assigned only one risk (the highest). Results with the 95% confidence intervals are summarized in the following table.

Study Subjects	Total	Positive Percent Agreement	95% Exact Confidence Interval	Negative Percent Agreement	95% Exact Confidence Interval
Overall	1207	99.5%* (435 / 437)	98.4, 99.9	99.0%* (762 / 770)	98.0, 99.6
Overall with signs or symptoms	142	100.0% (54 / 54)	93.4, 100.0	100.0% (88 / 88)	95.9, 100.0
Overall without signs or symptoms	1064	99.5%* (381 / 383)	98.1, 99.9	98.8%* (673 / 681)	97.7, 99.5
IVDU	456	99.3% (291 / 293)	97.6, 99.9	98.2% (160 / 163)	94.7, 99.6
Dialysis	6	100% (1 / 1)	2.5, 100.0	100.0% (5 / 5)	47.8, 100.0
Transfusion/Transplant	63	100.0% (16 / 16)	79.4, 100.0	100.0% (47 / 47)	92.5, 100.0
High Risk sex	461	100.0% (58 / 58)	93.8. 100.0	98.8 (398 / 403)	97.1, 99.6
HCV positive mother	2	100.0% (1 / 1)	2.5, 100.0	100.0% (1 / 1)	2.5, 100.0
Prior history of incarceration	56	100% (11 / 11)	71.5, 100.0	100.0% (45 / 45)	92.1, 100.0
HIV positive[§]	17	100.0 (2 / 2)	15.8, 100.0	100.0% 15 / 15	78.2, 100.0
None specified	3	100.0% (1 / 1)	2.5, 100.0	100.0% (2 / 2)	15.8, 100.0

*Includes subjects with "unable to determine" status.

[§]Does not include 377 additional HIV positive subjects enrolled but included in higher ranked risk categories, and 6 HIV positive subjects enrolled with signs or symptoms of hepatitis.

RESULTS OF SUPPLEMENTAL TESTING OF SPECIMENS REACTIVE IN THE ORAQUICK® HCV RAPID ANTIBODY TEST

The table below shows the results obtained when subjects reactive in the OraQuick® HCV Rapid Antibody Test were tested by recombinant immunoblot assay (RIBA®).

Number of OraQuick Reactive Results	RIBA® Results		
	Positive	Indeterminate	Negative
443	418	25*	0

*Seventeen (17) of the RIBA® indeterminate results were positive for HCV RNA when tested by PCR.

Of the subjects reactive in the OraQuick® HCV Rapid Antibody Test 94.4% (418/443) were positive by RIBA®. Seventeen (17) of the RIBA® indeterminate results were positive for HCV RNA when tested by PCR.

FINGERSTICK WHOLE BLOOD

Expected Results for the Intended Use Population

Of the 1670 fingerstick whole blood specimens tested in an OraQuick® HCV Rapid Antibody clinical study, 78.7% (1315/1670) were from subjects at risk for hepatitis C infection but were asymptomatic and reported no current signs or symptoms of hepatitis, and 21.3% (355/1670) were from subjects with current signs or symptoms of hepatitis. The 1670 individuals were enrolled from the following collection locations:

- 29.9% from Ft. Lauderdale, FL
- 15.2% from Miami, FL
- 9.8% from Allentown, PA
- 3.1% from Lebanon, NH
- 20.5% from New Bedford, MA
- 12.2% from Lexington, KY
- 9.3% from Baltimore, MD

A total of 1660 specimen results were included in the study analysis, as ten (10) OraQuick® results were excluded due to results read outside of the 20-40 minute read window. The OraQuick® HCV Rapid Antibody Test was reactive in 43.5% (722/1660) of subjects. There were no invalid OraQuick® HCV Rapid HCV Antibody Test results reported for the 1670 individuals tested (0% (0/1670) with 95% CI: 0.0% to 0.2%). Of the 1670 individuals tested, 26.6% (445/1670) were also self-reported HIV positive. The table below summarizes the distribution of OraQuick® HCV Rapid Antibody Test reactive, non-reactive, and invalid results for the 1660 subjects included in the analysis.

Age Range	Gender	OraQuick® HCV Rapid Antibody Test Results in High Risk Individuals – Fingerstick Whole Blood							
		No signs or symptoms				Signs or symptoms			
		Reactive	Non-Reactive	Invalid	Total (n)	Reactive	Non-Reactive	Invalid	Total (n)
		n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	
0-10	F	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
	M	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
11-19	F	3 (0.2)	8 (0.6)	0 (0.0)	11	0 (0.0)	6 (1.7)	0 (0.0)	6
	M	0 (0.0)	11 (0.8)	0 (0.0)	11	1 (0.2)	2 (0.6)	0 (0.0)	3
20-29	F	29 (2.2)	86 (6.6)	0 (0.0)	115	9 (2.5)	11 (3.1)	0 (0.0)	20
	M	25 (1.9)	73 (5.6)	0 (0.0)	98	5 (1.4)	9 (2.5)	0 (0.0)	14
30-39	F	31 (2.4)	65 (5.0)	0 (0.0)	96	9 (2.5)	13 (3.7)	0 (0.0)	22
	M	50 (3.8)	80 (6.1)	0 (0.0)	130	16 (4.5)	20 (5.6)	0 (0.0)	36
40-49	F	63 (4.8)	102 (7.8)	0 (0.0)	165	23 (6.5)	27 (7.6)	0 (0.0)	50
	M	109 (8.4)	184 (14.1)	0 (0.0)	293	46 (13.0)	28 (7.9)	0 (0.0)	74
50-59	F	48 (3.7)	46 (3.5)	0 (0.0)	94	18 (5.1)	13 (3.7)	0 (0.0)	31
	M	134 (10.3)	106 (8.1)	0 (0.0)	240	64 (18.0)	24 (6.8)	0 (0.0)	88
60-69	F	8 (0.6)	4 (0.3)	0 (0.0)	12	3 (0.8)	1 (0.3)	0 (0.0)	4
	M	21 (1.6)	18 (1.4)	0 (0.0)	39	7 (2.0)	0 (0.0)	0 (0.0)	7
70-79	F	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
	M	0 (0.0)	1 (0.1)	0 (0.0)	1	0 (0.0)	0 (0.0)	0 (0.0)	0
80-89	F	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
	M	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
90-100	F	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
	M	0 (0.0)	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0 (0.0)	0
Total (N)*		521 (40.0)	784 (60.0)	0 (0.0)	1305	201 (56.6)	154 (43.4)	0 (0.0)	355

*Excludes 10 subjects with OraQuick results read out of the 20-40 minute read window.

Venous Whole Blood Clinical Performance

A multi-center prospective study was conducted to evaluate the clinical performance of the OraQuick® HCV Rapid Antibody Test in fingerstick whole blood specimens from subjects with signs or symptoms of hepatitis and subjects at risk for hepatitis C infection. These risk factors included past or present intravenous drug use, having received a blood transfusion or organ transplant prior to 1992, evidence of high-risk sexual behavior, being born to an HCV positive mother, having been on long-term hemodialysis, history of incarceration, and positive for HIV. Clinical performance was evaluated in fingerstick whole blood specimens from subjects prospectively enrolled at 8 geographically dispersed centers within the United States. The population tested was Caucasian (53.1%), African American (40.6%), as well as a small proportion of other ethnic groups (6.3%). The mean age was 42.8 years (age range: 14 to 77 years). Of the 1660 subject specimens in the analysis population, 719 were HCV infected, 926 were negative, and 15 specimens had the status of "Unable to Determine". HCV status was determined for each subject by EIA, with supplemental RIBA® and PCR assays as required. The table below summarizes the distribution of OraQuick® HCV Rapid Antibody Test reactive, non-reactive, and invalid results in subjects with HCV infected status per the reference laboratory testing algorithm.

OraQuick® HCV Rapid Antibody Test Results	Subject HCV Infected Status		
	Positive	Negative	Unable to Determine Infected Status
Positive	708	3	11
Negative	11*	923	4
Invalid	0	0	0

*Six (6) of the eleven (11) were negative for HCV RNA by PCR.

Percent Positive and Negative Agreement Calculations

Percent positive and negative agreement between the OraQuick® HCV Rapid Antibody Test and HCV status were calculated overall for the analysis population (n=1660), as well as for subjects with signs or symptoms of hepatitis and subjects at risk for hepatitis C infection.

$$\text{Percent Positive Agreement} = \frac{\text{Number of OraQuick® HCV Rapid Antibody Test Reactive Results} \times 100}{\text{Total number of HCV Infected status}}$$

$$\text{Percent Negative Agreement} = \frac{\text{Number of OraQuick® HCV Rapid Antibody Test Non-Reactive Results} \times 100}{\text{Total number of HCV Not Infected status}}$$

For the purposes of calculating percent agreement, subjects reactive by the OraQuick HCV Rapid Antibody Test whose HCV status was "Unable to Determine" were considered "HCV Not Infected" and non-reactive subjects by the OraQuick HCV Rapid Test whose HCV status was "Unable to Determine" were considered "HCV Infected"

Percent Positive and Negative Agreement

The percent positive and negative agreement between the OraQuick® HCV Rapid Antibody Test and the subject HCV Infected Status were calculated for the analysis population (n=1660). Percent positive and negative agreement was also calculated for individuals with signs or symptoms of hepatitis, and for individuals at risk for hepatitis C infection. In addition, the percent positive and negative agreements according to risk factors for HCV infection were also calculated. The risks for HCV were ranked on a clinical evaluation of the likelihood of acquiring hepatitis C, with the most common given higher rankings.[3] Each subject was assigned only one risk (the highest ranking). Results with the 95% confidence intervals are summarized in the following tables.

Percent Positive Agreement and Percent Negative Agreement According to Risk

Study Subjects	Total	Percent Positive Agreement	95% Exact Confidence Interval	Percent Negative Agreement	95% Exact Confidence Interval
Overall	1660	97.9%* (708 / 723)	96.6%, 98.8%	98.5%* (923 / 937)	97.5%, 99.2%
Overall with signs and symptoms	355	99.0%* (197 / 199)	96.4%, 99.9%	97.4%* (152 / 156)	93.6%, 99.3%
Overall without signs or symptoms	1305	97.5%* (511 / 524)	95.8%, 98.7%	98.7%* (771 / 781)	97.7%, 99.4%
IVDU[€]	661	98.2% (428 / 436)	96.4%, 99.2%	97.3% (219 / 225)	94.3%, 99.0%
Dialysis	11	100.0% (2 / 2)	15.8%, 100.0%	100.0% (9 / 9)	66.4%, 100.0%
Transfusion / Transplant	48	92.3% (12 / 13)	64.0%, 99.8%	97.1% (34 / 35)	85.1%, 99.9%
High Risk Sex	502	96.5% (55 / 57)	87.9%, 99.6%	99.6% (443 / 445)	98.4%, 99.9%
HCV positive mother	5	No subjects met criteria	No subjects met criteria	100.0% (5 / 5)	47.8%, 100.0%
Prior history of incarceration	67	86.7% (13 / 15)	59.5%, 98.3%	98.1% (51 / 52)	89.7%, 100.0%
HIV positive[§]	11	100.0% (1 / 1)	2.5%, 100.0%	100.0% (10 / 10)	69.2%, 100.0%

*Includes subjects with "unable to determine" status.

[§]Does not include 314 additional HIV positive subjects enrolled but included in higher ranked risk categories, and 120 HIV positive subjects enrolled with signs or symptoms of hepatitis.

[€]Intravenous Drug User

Results of Supplemental Testing of Specimens Reactive in the OraQuick® HCV Rapid Antibody Test

The table below shows the results obtained when subjects reactive in the OraQuick® HCV Rapid Antibody Test were tested by recombinant immunoblot assay (RIBA®).

Number of OraQuick Reactive Results	RIBA®		
	Positive	Indeterminate	Negative
722[§]	690	29*	2

*Eighteen (18) of the RIBA® indeterminate results were positive for HCV RNA when tested by PCR.

[§] One (1) subject reactive by OraQuick did not have RIBA or PCR completed.

Of the subjects reactive in the OraQuick® HCV Rapid Antibody Test 95.6% (690/722) were positive by RIBA®. Eighteen (18) of the RIBA® indeterminate results were positive for HCV RNA when tested by PCR.

X. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Microbiology Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XI. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The data from the clinical and non-clinical studies demonstrated acceptable positive and negative percent agreement, seroconversion panel detection, and genotype detection of the OraQuick® HCV Rapid Antibody Test, when used according to the instructions for use in the labeling. The clinical studies in this application indicate that the OraQuick® HCV Rapid Antibody Test is safe and effective when used according to the directions for use in the labeling.

A. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

XII. CDRH DECISION

CDRH issued an approval order on February 18, 2011. The applicant's manufacturing facilities were inspected and found to be in compliance with the Quality System (QS) Regulation (21 CFR 820).

XIII. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XIV. REFERENCES

1. CDC, Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and other Bloodborne Pathogens in Health-Care Settings. MMWR 1988; 37(24):377-388.

2. CDC, Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis. MMWR 2001; 50 (RR-11):1-42.

3. CDC, Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV – Related Chronic Disease. MMWR 1998; 47(RR19): 1-39.